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518 Rec'd PCT/PTO 28 AUG 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application: Beerelli Seshi

National Phase of: PCT/US01/16408

International Filing Date: 21 May 2001

For: HUMAN MESENCHYMAL PROGENITOR CELL

Attorney Docket Number: 0152.00418

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231
Box PCT

Dear Sir:

Please preliminarily amend the above-captioned patent application prior to examination on the merits, consistent with the instructions found attached hereto:

IN THE SPECIFICATION:

CROSS-REFERENCE TO RELATED APPLICATIONS

This patent application is a National Phase Concerning a Filing Under 35 U.S.C. 371, claiming the benefit of priority of PCT/US01/16408, filed 21 May 2001, which claims the benefit of priority of United States Patent Application Numbers 60/277,700, filed 21 March 2001 and 60/209,245, filed 5 June 2001, all of which are incorporated herein by reference.

IN THE CLAIMS:

21. Isolated mesenchymal progenitor cells that are pluri-differentiated.
22. A therapeutic composition comprising an isolated pluri-differentiated mesenchymal progenitor cells and a pharmaceutically acceptable carrier, wherein said isolated pluri-differentiated mesenchymal progenitor cells are present in an amount effective for treating a disease state in a mammal in need thereof.
23. A therapeutic composition comprising isolated pluri-differentiated mesenchymal progenitor cells and a pharmaceutically acceptable carrier, wherein said pluri-differentiated mesenchymal progenitor cells are present in an amount effective to enhance hematopoietic progenitor cell engraftment in a mammal in need thereof.
24. A therapeutic composition comprising isolated pluri-differentiated mesenchymal progenitor cells and a pharmaceutically acceptable carrier, wherein said pluri-differentiated mesenchymal progenitor cells are present in an amount effective to treat GvHD in a mammal about to undergo bone marrow or organ transplantation or suffering from GvHD caused by bone marrow or organ transplantation.
25. A method for purifying pluri-differentiated mesenchymal progenitor cells comprising the steps of:

- a) providing a cell culture preparation by the Dexter method;
- b) treating the cells to obtain a cell suspension;
- c) removing macrophages;
- d) fractionating the cells; and
- e) collecting the fraction of pluri-differentiated mesenchymal progenitor cells.

26. A method for enhancing bone marrow engraftment in a mammal in need thereof which comprises administering to the mammal (i) isolated pluri-differentiated mesenchymal progenitor cells and (ii) a bone marrow graft, wherein the isolated pluri-differentiated mesenchymal progenitor cells are administered in an amount effective to promote engraftment of the bone marrow in the mammal.

27. The method according to claim 6, wherein said administering step includes intravenously injecting or directly injecting the isolated pluri-differentiated mesenchymal progenitor cells to the site of intended activity.

28. The method of claim 6 wherein the isolated pluri-differentiated mesenchymal progenitor cells are administered in a cell suspension also containing bone marrow graft cells.

29. The method according to claim 6, further including administering the isolated pluri-differentiated mesenchymal progenitor cells in a cell suspension also containing bone marrow graft cells.

30. A method for enhancing engraftment of hematopoietic progenitor cells in a mammal in need thereof which comprises administering to the mammal (i) isolated pluri-differentiated mesenchymal progenitor cells and (ii) hematopoietic progenitor cells, wherein the isolated pluri-differentiated mesenchymal progenitor cells are administered in an amount effective to promote engraftment of the hematopoietic progenitor cells in the mammal.

31. The method of claim **10**, wherein the isolated pluri-differentiated mesenchymal progenitor cells are administered by intravenous injection or by injecting directly to the site of intended activity.

32. The method of claim **10**, wherein the isolated pluri-differentiated mesenchymal progenitor cells are administered prior to administration of the hematopoietic progenitor cells.

33. The method of claim **10**, wherein the isolated pluri-differentiated mesenchymal progenitor cells are introduced in a cell suspension also containing hematopoietic progenitor cells.

34. A method for treating graft-versus-host disease (GvHD) in a mammal about to undergo bone marrow or organ transplantation or suffering from GvHD caused by bone marrow or organ transplantation, by administering to the mammal an effective amount of isolated pluri-differentiated mesenchymal progenitor cells.

35. The method according to claim **14**, wherein the mammal is one about to undergo allogeneic bone marrow transplantation or is suffering from GvHD caused by allogeneic bone marrow transplantation.

36. The method according to claim **14**, further including administering immunosuppressive drugs to the mammal.

37. The method according to claim **14**, wherein said isolated pluri-differentiated mesenchymal progenitor cells are administered by intravenous injection.

38. The method according to claim **14**, wherein the isolated pluri-differentiated mesenchymal progenitor cells are administered to said mammal prior to bone marrow or organ transplantation.

39. A method for diagnosing a disease state comprising the steps of:

- a) establishing gene expression patterns of normal state bone marrow derived isolated pluri-differentiated mesenchymal progenitor cells;
- b) establishing gene expression patterns of various leukemic state bone marrow derived isolated pluri-differentiated mesenchymal progenitor cells;
- c) identifying gene sets that are unique to a given state; and
- d) comparing a profile of bone marrow derived isolated mesenchymal progenitor cell of unknown state to said gene sets.

40. A method for identifying therapeutic targets for treatment of hematopoietic function comprising the steps of:

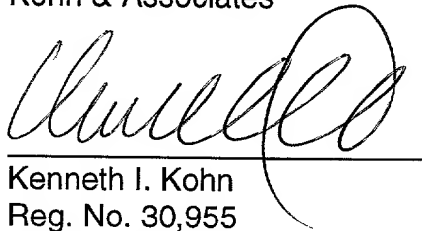
- a) determining the median gene expression profile of bone marrow isolated pluri-differentiated mesenchymal progenitor cells associated with each disease state of interest;
- b) identifying gene groups that are up-regulated, down regulated, and common to each disease state; and
- c) identifying gene sets that are unique to a given state.

REMARKS

The above amendments add no new matter and are merely made to more accurately describe and claim the invention, to claim benefit of priority, and to eliminate multiple claim dependencies.

Respectfully solicited,

Kohn & Associates

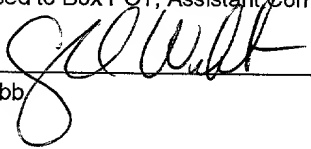


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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to Box PCT, Assistant Commissioner for Patents, Washington, D.C. 20231.


Angel Webb

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Page 1, after the Title, please insert the following section:

-- CROSS-REFERENCE TO RELATED APPLICATIONS

This patent application is a National Phase Concerning a Filing Under 35 U.S.C. 371, claiming the benefit of priority of PCT/US01/16408, filed 21 May 2001, which claims the benefit of priority of United States Patent Application Numbers 60/277,700, filed 21 March 2001 and 60/209,245, filed 5 June 2001, all of which are incorporated herein by reference. --

IN THE CLAIMS:

Please cancel claims 1-20.

21. (New) Isolated mesenchymal progenitor cells that are pluri-differentiated.
22. (New) A therapeutic composition comprising an isolated pluri-differentiated mesenchymal progenitor cells and a pharmaceutically acceptable carrier, wherein said isolated pluri-differentiated mesenchymal progenitor cells are present in an amount effective for treating a disease state in a mammal in need thereof.
23. (New) A therapeutic composition comprising isolated pluri-differentiated mesenchymal progenitor cells and a pharmaceutically acceptable carrier, wherein said pluri-differentiated mesenchymal progenitor cells are present in an amount effective to enhance hematopoietic progenitor cell engraftment in a mammal in need thereof.
24. (New) A therapeutic composition comprising isolated pluri-differentiated mesenchymal progenitor cells and a pharmaceutically acceptable carrier, wherein said pluri-differentiated mesenchymal progenitor cells are present in an amount effective to treat GvHD in a mammal about to undergo bone marrow or organ transplantation or suffering from GvHD caused by bone marrow or organ transplantation.

25. (New) A method for purifying pluri-differentiated mesenchymal progenitor cells comprising the steps of:

- a) providing a cell culture preparation by the Dexter method;
- b) treating the cells to obtain a cell suspension;
- c) removing macrophages;
- d) fractionating the cells; and
- e) collecting the fraction of pluri-differentiated mesenchymal progenitor cells.

26. (New) A method for enhancing bone marrow engraftment in a mammal in need thereof which comprises administering to the mammal (i) isolated pluri-differentiated mesenchymal progenitor cells and (ii) a bone marrow graft, wherein the isolated pluri-differentiated mesenchymal progenitor cells are administered in an amount effective to promote engraftment of the bone marrow in the mammal.

27. (New) The method according to claim 6, wherein said administering step includes intravenously injecting or directly injecting the isolated pluri-differentiated mesenchymal progenitor cells to the site of intended activity.

28. (New) The method of claim 6 wherein the isolated pluri-differentiated mesenchymal progenitor cells are administered in a cell suspension also containing bone marrow graft cells.

29. (New) The method according to claim 6, further including administering the isolated pluri-differentiated mesenchymal progenitor cells in a cell suspension also containing bone marrow graft cells.

30. (New) A method for enhancing engraftment of hematopoietic progenitor cells in a mammal in need thereof which comprises administering to the mammal (i) isolated pluri-differentiated mesenchymal progenitor cells and (ii) hematopoietic progenitor cells, wherein the isolated pluri-differentiated mesenchymal progenitor cells are administered

in an amount effective to promote engraftment of the hematopoietic progenitor cells in the mammal.

31. (New) The method of claim **10**, wherein the isolated pluri-differentiated mesenchymal progenitor cells are administered by intravenous injection or by injecting directly to the site of intended activity.

32. (New) The method of claim **10**, wherein the isolated pluri-differentiated mesenchymal progenitor cells are administered prior to administration of the hematopoietic progenitor cells.

33. (New) The method of claim **10**, wherein the isolated pluri-differentiated mesenchymal progenitor cells are introduced in a cell suspension also containing hematopoietic progenitor cells.

34. (New) A method for treating graft-versus-host disease (GvHD) in a mammal about to undergo bone marrow or organ transplantation or suffering from GvHD caused by bone marrow or organ transplantation, by administering to the mammal an effective amount of isolated pluri-differentiated mesenchymal progenitor cells.

35. (New) The method according to claim **14**, wherein the mammal is one about to undergo allogeneic bone marrow transplantation or is suffering from GvHD caused by allogeneic bone marrow transplantation.

36. (New) The method according to claim **14**, further including administering immunosuppressive drugs to the mammal.

37. (New) The method according to claim **14**, wherein said isolated pluri-differentiated mesenchymal progenitor cells are administered by intravenous injection.

38. (New) The method according to claim **14**, wherein the isolated pluri-differentiated mesenchymal progenitor cells are administered to said mammal prior to bone marrow or organ transplantation.

39. (New) A method for diagnosing a disease state comprising the steps of:

- a) establishing gene expression patterns of normal state bone marrow derived isolated pluri-differentiated mesenchymal progenitor cells;
- b) establishing gene expression patterns of various leukemic state bone marrow derived isolated pluri-differentiated mesenchymal progenitor cells;
- c) identifying gene sets that are unique to a given state; and
- d) comparing a profile of bone marrow derived isolated mesenchymal progenitor cell of unknown state to said gene sets.

40. (New) A method for identifying therapeutic targets for treatment of hematopoietic function comprising the steps of:

- a) determining the median gene expression profile of bone marrow isolated pluri-differentiated mesenchymal progenitor cells associated with each disease state of interest;
- b) identifying gene groups that are up-regulated, down regulated, and common to each disease state; and
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